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## **Influenza epidemiology in patients admitted to sentinel Australian hospitals in 2019: the Influenza Complications Alert Network (FluCAN)**

Allen C Cheng, Dominic E Dwyer, Mark Holmes, Louis B Irving, Graham Simpson, Sanjaya Senanayake, Tony Korman, N Deborah Friedman, Louise Cooley, Peter Wark, Anna Holwell, Simon Bowler, John W Upham, Daniel M Fatovich, Grant W Waterer, Kristine Macartney, Christopher C Blyth, Nigel Crawford, Jim Buttery, Helen S Marshall, Julia E Clark, Joshua Francis, Tom Kotsimbos, Paul M Kelly

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## Annual report

# Influenza epidemiology in patients admitted to sentinel Australian hospitals in 2019: the Influenza Complications Alert Network (FluCAN)

Allen C Cheng, Dominic E Dwyer, Mark Holmes, Louis B Irving, Graham Simpson, Sanjaya Senanayake, Tony Korman, N Deborah Friedman, Louise Cooley, Peter Wark, Anna Holwell, Simon Bowler, John W Upham, Daniel M Fatovich, Grant W Waterer, Kristine Macartney, Christopher C Blyth, Nigel Crawford, Jim Buttery, Helen S Marshall, Julia E Clark, Joshua Francis, Tom Kotsimbos, Paul M Kelly

## Abstract

Influenza is a common cause of acute respiratory infection, and is a major cause of morbidity and mortality. This report summarises the epidemiology of hospitalisations with laboratory-confirmed influenza during the 2019 influenza season.

The Influenza Complications Alert Network (FluCAN) is a sentinel hospital-based surveillance program that operates at sites in all jurisdictions in Australia. Cases were defined as patients hospitalised at any of the 17 sentinel hospitals with influenza confirmed by nucleic acid detection. Data were also collected on a frequency matched control group of influenza-negative patients admitted with acute respiratory infection.

During the period 1 April to 31 October 2019 (the 2019 influenza season), there were 4,154 patients admitted with confirmed influenza to one of 17 FluCAN sentinel hospitals. Of these, 44% were elderly ( $\geq 65$  years), 21% were children ( $< 16$  years), 7.7% were Aboriginal and Torres Strait Islander peoples, 1.7% were pregnant and 73% had chronic comorbidities. Most admissions were due to influenza A infection (85%). Estimated vaccine coverage was 75% in the elderly, 49% in non-elderly adults with medical comorbidities, and 27% in young children ( $< 5$  years). The estimated vaccine effectiveness in the target adult population was 42% (95% confidence interval [95% CI]: 36%, 49%).

There were a larger number of hospital admissions detected with confirmed influenza in this national observational surveillance system in 2019 than in 2018.

Keywords: Influenza; public health surveillance; influenza vaccines; vaccination coverage; vaccine effectiveness

## Introduction

Influenza is an acute respiratory viral infection caused by influenza viruses. Global studies suggest that along with respiratory syncytial virus (RSV), influenza A and B are the most common viruses identified in surveillance systems,<sup>1</sup> and it has been estimated that influenza caused 9.5 million hospitalisations and 145,000 deaths in 2017.<sup>2</sup> In Australia, an analysis of administrative hospital data found that influenza is diagnosed in up to 10,000 admissions annually, with the

highest incidence in children and the elderly.<sup>3</sup> In this report, we describe the epidemiology of hospitalisation with laboratory-confirmed influenza in the 2019 season in Australia.

## Methods

The Influenza Complications Alert Network (FluCAN) is a national hospital-based sentinel surveillance system.<sup>4–6</sup> Since 2011, the participating sites have been:

- Canberra Hospital (Australian Capital Territory, ACT)
- Calvary Hospital (ACT)
- Westmead Hospital (New South Wales, NSW)
- John Hunter Hospital (NSW)
- Children's Hospital at Westmead (NSW)
- Alice Springs Hospital (Northern Territory, NT)
- Mater Hospital (Queensland, Qld)
- Princess Alexandra Hospital (Qld)
- Cairns Base Hospital (Qld)
- Royal Adelaide Hospital (South Australia, SA)
- Royal Hobart Hospital (Tasmania, Tas.)
- The Alfred Hospital (Victoria, Vic.)
- Royal Melbourne Hospital (Vic.)
- Monash Medical Centre (Vic.)
- University Hospital Geelong (Vic.)
- Royal Perth Hospital (Western Australia, WA)
- Perth Children's Hospital (previously Princess Margaret Hospital, WA).

In 2018, additional specialist paediatric hospitals—(Queensland Children's Hospital (previously Lady Cilento Children's Hospital, Qld), Women's and Children's Hospital (SA), the paediatric ward of the Royal Darwin Hospital (NT) and Royal Children's Hospital (Vic.)—also contributed data, but data from these sites were only included to estimate vaccine effectiveness to facilitate comparisons with previous years (Figure 1). Ethical approval has been obtained at all participating sites and at Monash University. Hospital bed capacity statistics were obtained from each participating hospital, and national bed capacity was obtained from the last published Australian Institute of Health and Welfare (AIHW) report.<sup>7</sup>

An influenza case was defined as a patient admitted to hospital with influenza confirmed by nucleic acid testing (NAT). Surveillance is conducted from early April to the end of October (with follow-up continuing to the end of November) each year. Data on a frequency-matched group of test-negative controls were also collected. Admission or transfer to an

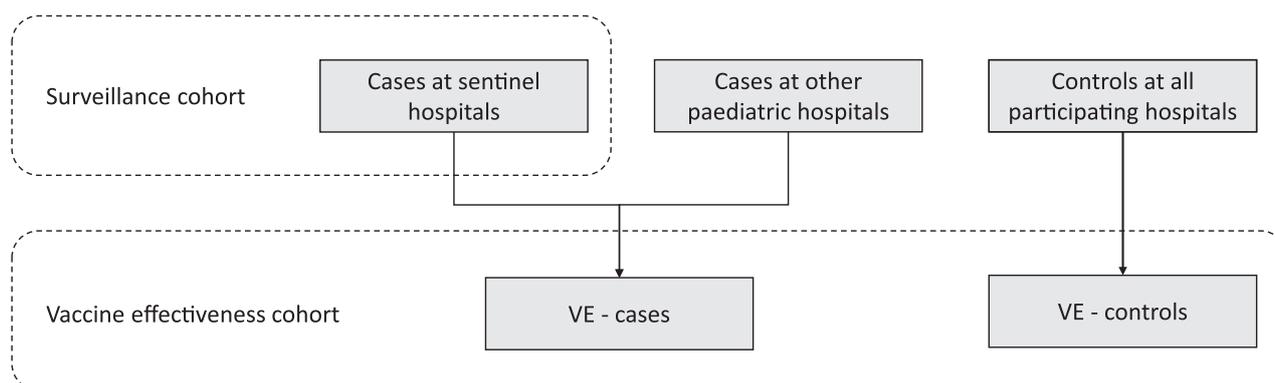
intensive care unit (ICU) included patients managed in a high dependency unit (HDU). The onset date was defined as the date of admission except for patients where the date of the test was more than seven days after admission, where the onset date was the date of the test. The presence of risk factors and comorbidities was ascertained from the patient's medical record. Restricted functional capacity was defined as those who were not fully active and not able to carry out all activities without restriction prior to the acute illness.<sup>8</sup>

We examined factors associated with ICU admission using multivariable regression. Factors independently associated with ICU admission were determined using a logistic regression model with no variable selection process, as all included factors were plausibly related to ICU admission.

The presentation delay was defined as the time from onset of illness to admission to hospital. The treatment delay was defined as the time from onset of illness to prescription of oseltamivir (in patients that received treatment). Patients were categorised into those that (a) did not receive oseltamivir; (b) received oseltamivir within two days of symptom onset; and (c) received oseltamivir more than two days after symptom onset. We modelled factors associated with length of hospital stay, including antiviral use, using a negative binomial regression, where the exponential of the regression coefficient represents the relative increase in hospital length of stay.

Vaccine coverage was estimated from the proportion of vaccinated individuals in test negative controls in each age group, stratified by the presence of chronic comorbidities. Vaccine effectiveness  $\epsilon$  was estimated from  $\theta$ , the odds ratio of vaccination in cases versus controls, using the formula  $\epsilon = 1 - \theta$  with the odds ratio calculated from a conditional logistic regression, stratified by site and month and adjusted for age group, the presence of chronic comorbidities, pregnancy and Aboriginal or Torres Strait Islander ethnicity.

**Figure 1: Participants included in surveillance and vaccine effectiveness cohorts**



## Results

During the period 1 April to 31 October 2019, there were 4,154 patients admitted with laboratory-confirmed influenza to the 17 FluCAN sentinel hospitals. The peak weekly number of admissions was in mid-August (week 27) (Figure 2). The majority of cases were due to influenza A ( $n = 3,537$ , 85.1%). The proportion due to influenza B varied across jurisdictions, ranging from 3.3% in Tasmania and 4.3% in SA to 24.3% in NSW and 24.4% in WA.

Of the 4,154 patients admitted with confirmed influenza, 1,850 (44.5%) were elderly (> 65 years of age); 883 (21.3%) were children (< 16 years of age); 319 (7.7%) were Aboriginal and Torres Strait Islander peoples; and 3,023 (72.8%) had chronic comorbidities (Table 1, Table 2). There were 69 pregnant women, representing 15.0% of the 461 female patients aged 16–49, or 1.7% of the total. Of the 3,458 patients (83.2%) for whom influenza vaccination status was ascertained, 1,658/3,458 (47.9%) had been vaccinated.

### Incidence of hospital admissions with influenza

Overall, the peak incidence of admissions with confirmed influenza was 4.5 per 100 hospital beds (Figure 3; in epidemiological week 27), but varied from a high of 23.3 weekly admissions per 100 hospital beds at the Alice Springs Hospital to a low of 0.4 per 100 hospital beds at Princess Alexandra Hospital (Figure 4).

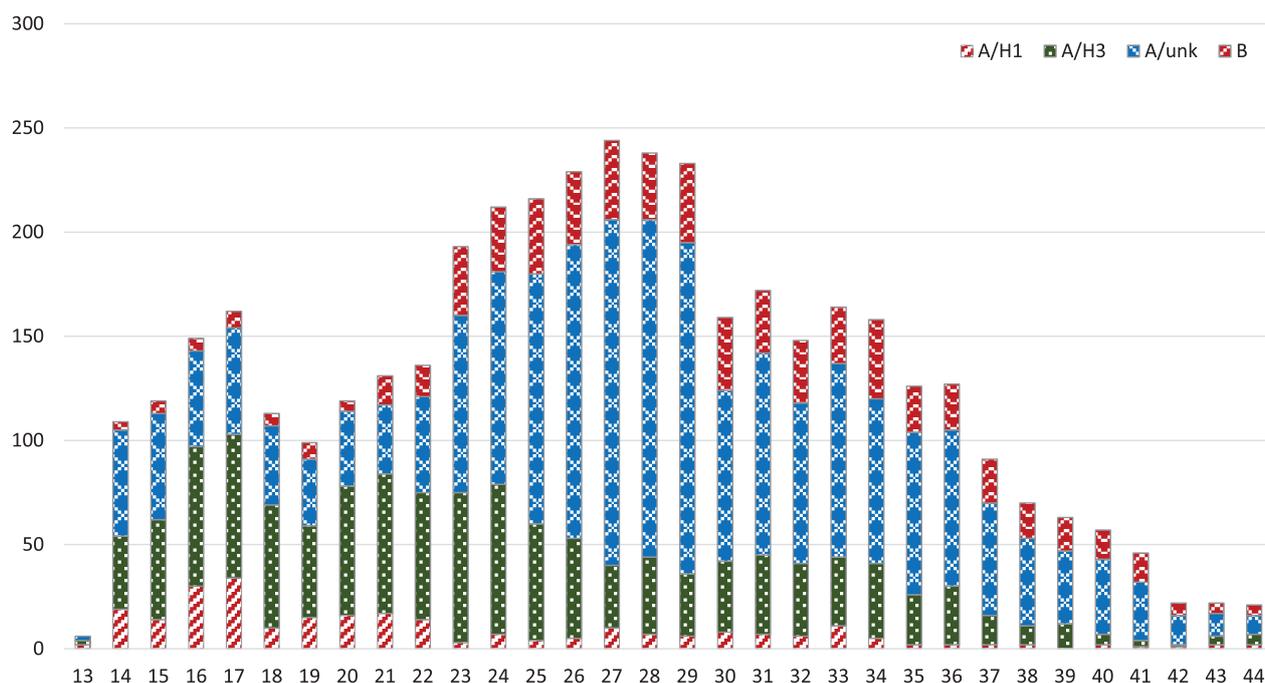
## Presentation and management

Of all cases, 3,960 patients had a known date of onset of illness documented. Of these, 200 cases (5.1%) were diagnosed more than seven days after admission and therefore were likely to be hospital-acquired. For the remaining 3,760 patients with community-onset laboratory-confirmed influenza where the duration of symptoms was known, the median duration of symptoms prior to admission was three days (interquartile range (IQR): 1, 5 days). In 2,721 patients that received antivirals, the delay from onset of illness to admission was more than two days in 56.7% ( $n = 1,544$ ), and was similar in children (54.4%), non-elderly adults (59.0%) and the elderly (62.4%).

Radiological evidence of pneumonia was present in 641 patients (15.4%). The proportion of patients with pneumonia was lower in children (9.6%) than in non-elderly adults (15.3%) and elderly adults (18.3%). A higher proportion of patients with pneumonia were admitted to ICU (20.1%) than those without pneumonia (5.5%).

Of all cases, 323 (7.8%) patients were admitted to ICU, comprising 259 patients (6.2%) initially admitted to ICU and a further 64 (1.5%) subsequently transferred to ICU after initial admission to a general ward. Non-elderly adults, those admitted with A/H1N1 infection and those with chronic comorbidities were more likely to be admitted to ICU; residents of nursing homes were less likely to be admitted to ICU (Table 3).

**Figure 2: Date of admission in patients hospitalised with confirmed influenza, 2019<sup>a</sup>**



a By week beginning on listed date; representing date of admission (or date of influenza diagnosis if acquired after more than seven days in hospital).

## Use of antivirals

Of the 3,621 patients where the date of onset was reported, 1,173 (32.4%) did not receive oseltamivir; 961 (26.5%) received oseltamivir within 2 days of symptom onset; and 1,447 (40.0%) received oseltamivir more than 2 days after the onset of illness. Oseltamivir use was lower in children (18.4% within 2 days; a further 21.9% more than 2 days) than in non-elderly adults (29.5%; 42.3%) and the elderly (29.5%; 49.1%) (table 4).

## Outcome

The mean length of hospital stay for all patients was 4.9 days. Admission to ICU was associated with a mean hospital length of stay of 9.5 days compared to those not admitted to ICU (4.5 days). Of the 3,956 patients where hospital mortality status was documented, 111 patients died (2.8%); of these, 34 deaths (31%) occurred in patients admitted to ICU, and 77 deaths (69%) in those not admitted to ICU.

Length of hospital stay was shorter in patients who did not receive oseltamivir (median 2 days; IQR: 1, 4 days) than in those who received oseltamivir within two days (median 3 days; IQR: 2, 6 days) or in those who received oseltamivir after two days (median 3 days; IQR: 2, 6 days; Kruskal–Wallis test  $p < 0.001$ ). The crude association between oseltamivir use and longer length of hospital stay was largely accounted for by age, the severity of illness and the presence of comorbidities in a multivariate model (Table 5).

## Vaccine coverage and effectiveness

A cohort to estimate vaccine effectiveness included 4,154 cases at the 17 surveillance hospitals together with 1,180 cases at additional paediatric hospitals (Figure 1). Vaccination status was ascertained in 4,617 of 5,334 cases (86.6%) and 3,083 of 3,678 test-negative control patients (83.8%).

Estimated vaccine coverage was 75.3% (683/907) in the elderly ( $\geq 65$  years) and 46.9% (285/608) in non-elderly adults with medical comorbidities.

**Table 1: Demographic characteristics of hospitalized patients with confirmed influenza**

	Influenza type/subtype				Total
	A/H1N1	A/H3N2	A/unknown	B	
Number	266	1,140	2,131	617	4,154
<b>Age group</b>					
< 16 years	53 (19.9%)	187 (16.4%)	299 (14.0%)	344 (55.8%)	883 (21.3%)
16–49 years	85 (32.0%)	168 (14.7%)	438 (20.6%)	137 (22.2%)	828 (19.9%)
50–64 years	58 (21.8%)	155 (13.6%)	323 (15.2%)	57 (9.2%)	593 (14.3%)
65–79 years	51 (19.2%)	298 (26.1%)	519 (24.4%)	52 (8.4%)	920 (22.1%)
80+ years	19 (7.1%)	332 (29.1%)	552 (25.9%)	27 (4.4%)	930 (22.4%)
Male	148 (55.6%)	566 (49.6%)	1,034 (48.5%)	307 (49.8%)	2,055 (49.5%)
Pregnant	4 (1.5%)	15 (1.3%)	39 (1.8%)	11 (1.8%)	69 (1.7%)
Aboriginal and Torres Strait Islander persons	40 (15.0%)	110 (9.6%)	120 (5.6%)	49 (7.9%)	319 (7.7%)
<b>Jurisdiction</b>					
ACT	33 (12.4%)	29 (2.5%)	481 (22.6%)	67 (10.9%)	610 (14.7%)
NSW	67 (25.2%)	244 (21.4%)	406 (19.1%)	230 (37.3%)	947 (22.8%)
NT	38 (14.3%)	96 (8.4%)	8 (0.4%)	13 (2.1%)	155 (3.7%)
Qld	8 (3.0%)	36 (3.2%)	198 (9.3%)	61 (9.9%)	303 (7.3%)
SA	33 (12.4%)	253 (22.2%)	67 (3.1%)	16 (2.6%)	369 (8.9%)
Tas.	15 (5.6%)	209 (18.3%)	13 (0.6%)	8 (1.3%)	245 (5.9%)
Vic.	45 (16.9%)	81 (7.1%)	823 (38.6%)	108 (17.5%)	1,057 (25.4%)
WA	27 (10.2%)	192 (16.8%)	135 (6.3%)	114 (18.5%)	468 (11.3%)

Of the elderly patients without influenza who had received influenza vaccine and the vaccine type was known, 92.1% (500/543) were vaccinated with adjuvanted trivalent influenza vaccine (TIV), 2.7% (15/543) were vaccinated with high-dose TIV, and 5.2% (28/543) were vaccinated with quadrivalent influenza vaccine (QIV). Of the 1,799 participants aged > 65 years (both cases and controls) where vaccination status was ascertained, 1,123 (62.4%) were recorded in the Australian Immunisation Register. In children within the 6 months – 4 years age group, estimated vaccine coverage was 27.1% (247/910), and in children aged 5–15 years the estimated coverage was 20.1% (167/831).

In adults who were elderly and/or had chronic medical conditions, the adjusted odds ratio of vaccination was 0.57 (95% CI: 0.51, 0.65). The

estimated vaccine effectiveness in the target adult population was therefore 42% (95% CI: 36%, 49%). In the elderly (> 65 years), estimated vaccine effectiveness was lower (VE 29%, 95% CI: 11%, 43%). The estimated vaccine effectiveness (versus no vaccine) of adjuvanted TIV was 32% (95% CI: 12, 48%); the number of cases > 65 years who received high-dose TIV or standard QIV was too small for meaningful analysis.

## Discussion

This report has documented a high number of cases in the FluCAN sentinel sites during 2019, comparable with the total number of cases reported in 2017. Based on the number of FluCAN hospital beds relative to the national bed capacity, this is estimated to represent more than 30,000 admissions across the country.

**Table 2: Risk factors, severity and outcomes in hospitalized adult patients with confirmed influenza**

	Not admitted to ICU	Admitted to ICU	Total
	n (%)	n (%)	
Number of patients	3,831 (92.2%)	323 (7.8%)	4,154
Pregnant	64 (92.8%)	5 (7.2%)	69
Chronic comorbidities	2,762 (91.4%)	261 (8.6%)	3,023
Chronic respiratory illness	1,150 (90.3%)	123 (9.7%)	1,273
Diabetes	746 (90.5%)	78 (9.5%)	824
Chronic liver disease	163 (88.1%)	22 (11.9%)	185
Immunosuppressed	572 (91.8%)	51 (8.2%)	623
Malignancy	337 (92.3%)	28 (7.7%)	365
Chronic cardiac disease	1,119 (90.2%)	121 (9.8%)	1,240
Obesity	341 (86.5%)	53 (13.5%)	394
Chronic neurological illness	728 (91.7%)	66 (8.3%)	794
Chronic renal disease	498 (91.4%)	47 (8.6%)	545
Nursing home resident	275 (97.9%)	6 (2.1%)	281
Received influenza vaccine	1,544 (93.1%)	114 (6.9%)	1,658
<b>Influenza subtype</b>			
A/H1	225 (84.6%)	41 (15.4%)	266
A/H3	1,057 (92.7%)	83 (7.3%)	1,140
A/unknown	1,964 (92.2%)	167 (7.8%)	2,131
B	585 (94.8%)	32 (5.2%)	617
In-hospital mortality <sup>a</sup>	77/3,664 (CFR: 2.1%)	34/292 (CFR: 11.6%)	111/3,956 (CFR: 2.8%)

a CFR: case fatality ratio.

Confirmed cases are likely to be an underestimate of the true burden of severe influenza in the participating sites for several reasons; the early start to the 2019 season meant that many cases may have presented prior to the commencement of surveillance in April. Additionally, not all cases of influenza are diagnosed, particularly those with delayed presentations of influenza-related complications (such as secondary bacterial pneumonia) and non-respiratory complications (such as encephalopathy or acute myocardial infarction).

There were significant differences in the timing and duration of the influenza season across different jurisdictions, with the Northern Territory, Queensland and South Australia having early activity; Western Australia having a short spike in cases; and the Australian Capital Territory,

New South Wales, Tasmania and Victoria having a prolonged duration of elevated influenza activity. A previous study has compared FluCAN's interim case counts with those of other surveillance systems and has noted that intensity varies between southern hemisphere countries.<sup>9</sup> The 2019 season was dominated by the A/H3N2 subtype, with smaller proportions due to A/H1N1 and influenza B infection.

There has been speculation about the impact of increased use of point of care testing on notified influenza cases that became increasingly available in 2018.<sup>10</sup> The hospitals that participate in FluCAN have had mostly-unchanged access to nucleic acid testing over many years, and testing in hospital inpatients is generally encouraged due to clinical and infection control implications. The data reported here therefore

**Figure 3: Incidence of confirmed influenza (per 100 influenza tests and per 1000 admissions) by epidemiological week, 2019**



suggest that the increased reported case numbers in 2019, compared to 2018, represent a real increase in the incidence rate of severe influenza, with hospital activity comparable to 2017. However, the possibility cannot be excluded that increased awareness amongst clinicians may have led to increased testing.

The peak rate of influenza hospitalisations relative to hospital bed capacity provides a measure of impact. The peak rate of admissions overall was 4.5 per 100 beds/week in week 27, lower than in 2017 where peak admissions were 5.9 per 100 beds/week in week 35. Notably the two Northern Territory hospitals (Alice Springs Hospital and the paediatric ward of the Royal Darwin Hospital) had the highest peak rate of influenza admissions. Based on a mean length of hospital stay of 4.9 days, this suggests that 3.2% of hospital beds were occupied with patients with confirmed influenza during that week.

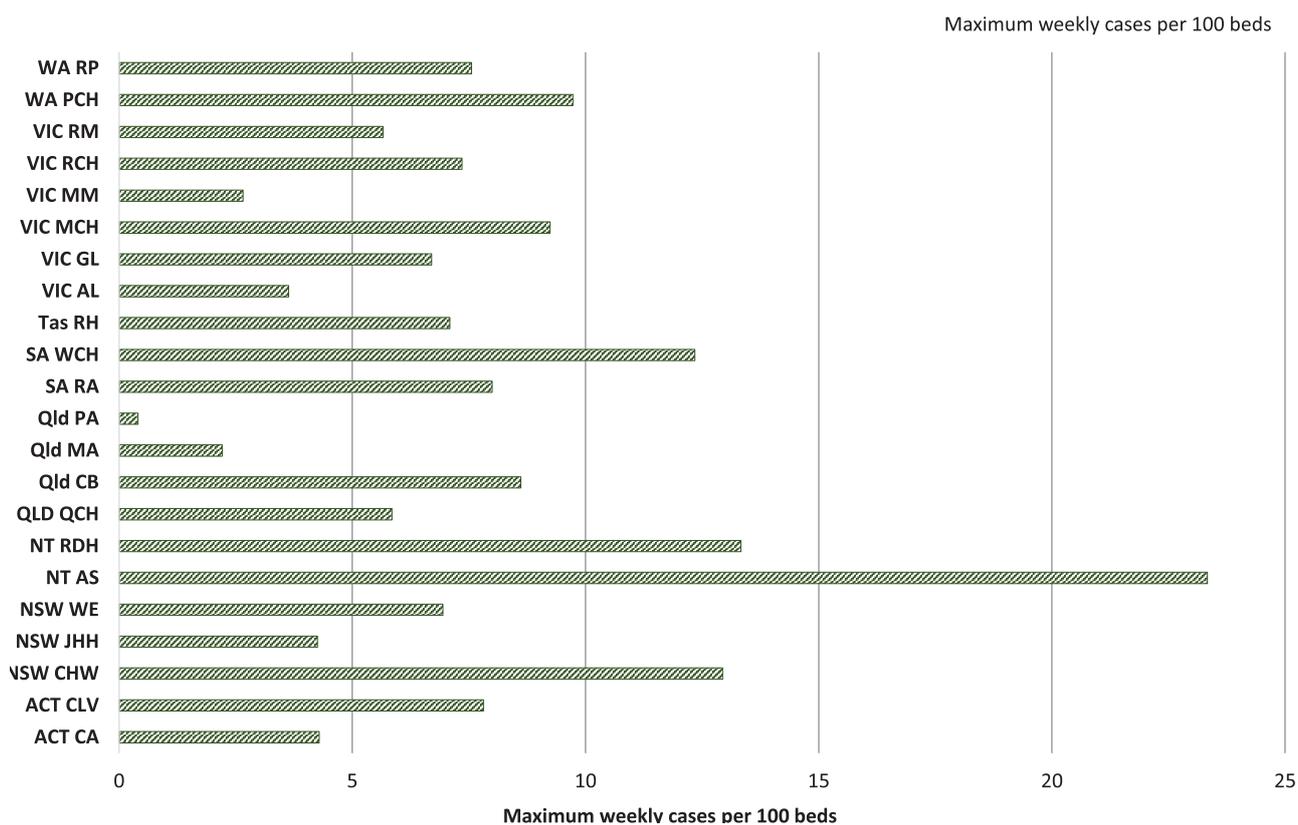
In 2019, there was a change to the funding arrangements for enhanced influenza vaccines for older Australians. In contrast to 2018, when

both the adjuvanted (Fluad, Seqirus) and high dose (Fluzone HD, Sanofi) vaccines were available,<sup>11</sup> in 2019, only the adjuvanted vaccine was available under the National Immunisation Program, while the high-dose vaccine was only available on the private market. As expected, the majority of those over 65 years of age received the adjuvanted influenza vaccine.

Jurisdictional paediatric influenza vaccine programs for children aged 6 months – 4 years were initiated in 2018 and continued in 2019. These will be funded under the National Immunisation Program in 2020. The impact of this program is yet to be formally evaluated, but is likely to be positive given good vaccine effectiveness and improving vaccine coverage. Although complications are rare, at a population level, influenza causes hospitalisations, severe complications and mortality in this patient group.<sup>3,12</sup>

Estimates of influenza vaccine coverage obtained from the present report are higher than estimates made from the Australian Immunisation Register (AIR). Based on AIR data, estimated

Figure 4: Peak incidence of confirmed influenza (per 100 hospital beds per week) by hospital<sup>a</sup>



a CA: Canberra Hospital; CLV: Calvary Hospital; CHW: Children’s Hospital at Westmead; JHH: John Hunter Hospital; WE: Westmead Hospital; AS: Alice Springs Hospital; RDH: Royal Darwin Hospital; QCH: Queen’s Children Hospital; CB: Cairns Base Hospital; MA: Mater Hospital; PA: Princess Alexandra Hospital; RA: Royal Adelaide; WCH: Women’s and Children’s Hospital; RH: Royal Hobart Hospital; AL: The Alfred Hospital; GL: University Hospital Geelong; MCH: Monash Children’s Hospital; MM: Monash Medical Centre; RCH: Royal Children’s Hospital; RM: Royal Melbourne; PCH: Perth Children’s Hospital; RP: Royal Perth Hospital.

coverage in children aged 6 months – 4 years was 5.6% in 2017 and at 26.2% in 2018.<sup>13</sup> In adults, estimated coverage in people aged 18–49 years was 8.9%; in those aged 50–64 years, coverage was 17.2%; and in those aged ≥ 65 years it was 46.3%.<sup>14</sup> In contrast, surveys and surveillance systems have consistently found higher coverage.<sup>5,6,15</sup> Although estimated coverage in older Australians > 65 years has been similar, there was a change in the vaccine formulation received, consistent with the change in funding status for the high-dose vaccine. However, it is difficult to reconcile the present report’s estimates of relatively stable vaccine coverage with distribution data which suggested an increase in doses supplied by around 13% since 2018.<sup>16</sup> The capture of the AIR in vaccinated cases and controls > 65 years increased from 48% in 2018 to 62% in 2019.

Estimates of vaccine effectiveness are likely to vary due to differences in circulating strains, target populations, methodology and, potentially, the vaccine types used. The most recently-reported estimates from the northern hemisphere were from the 2018/2019 season dominated by A/H1N1, where vaccine effectiveness has been higher than against A/H3N2. These include primary-care based estimates in the United States of America (47%; 95% CI: 34–57%),<sup>17</sup> Europe (32–43% in different systems),<sup>18</sup> and Canada (72%; 95% CI: 60–81% against A/H1N1),<sup>19</sup> and a Danish hospital-based system (38%; 95% CI: 24–49%).<sup>18</sup> A recent study has reported heterogeneous interim estimates in southern hemisphere systems.<sup>9</sup> The present report’s estimates of vaccine effectiveness in the target population are relatively high when compared to previous seasons where A/H3N2 has dominated.

**Table 3: Factors associated with admission to intensive care in patients hospitalised with confirmed influenza**

Variable	Crude OR <sup>a</sup>	p value	Adjusted OR <sup>a,b</sup>	p value
<b>Age</b>				
< 16 years	0.48 (0.34, 0.67)	< 0.01	0.51 (0.34, 0.75)	< 0.01
16–64 years	1		1	
65+ years	0.62 (0.48, 0.79)	< 0.01	0.59 (0.45, 0.78)	< 0.01
<b>Medical comorbidities</b>				
Aboriginal or Torres Strait Islander peoples	1.15 (0.77, 1.73)	0.49	0.89 (0.58, 1.36)	0.58
Pregnancy	0.93 (0.37, 2.32)	0.87	0.58 (0.23, 1.46)	0.25
Restricted functional status	1.11 (0.88, 1.40)	0.38	0.81 (0.62, 1.05)	0.12
<b>Influenza type/subtype</b>				
A/H1	3.33 (2.05, 5.42)	< 0.01	2.67 (1.61, 4.41)	< 0.01
A/H3	1.44 (0.94, 2.19)	0.09	1.30 (0.84, 2.03)	0.24
A/unk	1.55 (1.05, 2.29)	0.03	1.41 (0.93, 2.12)	0.10
B	1		1	

a OR: odds ratio.

b All variables included in multivariate model.

**Table 4: Oseltamivir treatment, by age group in patients with confirmed influenza**

Factor	Age < 16 years	Age 16–64 years	Age 65+ years	p value
<b>Number of patients</b>	<b>855</b>	<b>1,171</b>	<b>1,595</b>	
Oseltamivir not received	511 (59.8%)	325 (28.2%)	337 (21.4%)	< 0.001 <sup>b</sup>
Oseltamivir received	344 (40.2%)	826 (71.8%)	1,238 (78.6%)	
• received < 48h of onset	157 (18.4%)	339 (29.5%)	465 (29.5%)	
• received ≥ 48h of onset	187 (21.9%)	487 (42.3%)	773 (49.1%)	
Delay between onset and admission, in days, median (IQR)	3 (1, 5)	3 (1, 5)	3 (2, 4)	0.55
Delay between onset and treatment, <sup>a</sup> in days, median (IQR)	3 (2, 5)	3 (2, 5)	3 (2, 5)	0.100
Length of stay, in days, median (IQR)	1 (1, 2)	2 (1, 4)	4 (2, 7)	

a Of patients who received oseltamivir.

b This p value refers to a chi squared test for the categories oseltamivir not received / oseltamivir received within 48 hr of onset / oseltamivir received more than 48 hr after onset, with a null hypothesis that proportions within each category are equal across all age groups.

Data suggest that influenza vaccination of elderly adults averts 10–15% of confirmed influenza in primary care in US and European studies.<sup>20–22</sup> A previous FluCAN report has estimated that influenza vaccination averted 50% of hospital admissions with confirmed influenza in the elderly, 41% in non-elderly adults with comorbidities and 25% in children,<sup>23</sup> although these proportions would be expected to vary with

vaccine effectiveness and coverage. A recent study has found that the influenza vaccine protects against fatal hospital admission with confirmed influenza by 31%.<sup>24</sup>

The ALIC4E trial, a clinical trial of oseltamivir in elderly patients in primary care conducted independently of pharmaceutical sponsorship, was recently reported.<sup>25</sup> The trial confirmed

**Table 5: Factors associated with length of stay in patients with confirmed influenza**

Variable	Crude rate ratio <sup>a</sup>	p value	Adjusted rate ratio <sup>a</sup>	p value
<b>Oseltamivir treatment</b>				
No oseltamivir	1 (referent)		1 (referent)	
received < 48h of onset	1.35 (1.03, 1.76)	0.03	1.12 (0.91, 1.38)	0.273
received ≥ 48h of onset	1.42 (1.06, 1.90)	0.018	1.10 (0.89, 1.36)	0.354
<b>Age group</b>				
< 16 years	0.54 (0.39, 0.75)	< 0.001	0.64 (0.49, 0.84)	0.039
16–64 years	1 (referent)		1 (referent)	
65+ years	1.30 (1.09, 1.57)	0.004	1.27 (1.07, 1.52)	0.008
<b>Comorbidities</b>				
ICU admission	1.90 (1.53, 2.35)	< 0.001	1.51 (1.29, 1.77)	< 0.001
	2.12 (1.78, 2.53)	< 0.001	2.09 (1.84, 2.36)	< 0.001

a Represents relative difference in length of stay; rate ratio (RR) > 1 indicates longer stay associated with factor.

previous findings that oseltamivir is associated with an improvement of around 24 hours in the time to recovery. However, it found that benefits were greater in the elderly; in those with chronic comorbidities; and in those with an increased severity of symptoms. Interestingly, the trial also suggested that patients with delayed presentations of more than 48–72 hours also appeared to benefit.

Although the ALIC4E trial was based in primary care, its finding is of relevance to hospitalized patients who tend to be older, to have chronic comorbidities, to have severe illness and to present later in the course of illness. Unfortunately, despite enrolling 3,266 patients, the ALIC4E trial was underpowered to detect differences in complications of influenza relevant for public health policy, such as hospitalisation and death. National guidelines continue to recommend use of oseltamivir based on observational studies.<sup>26</sup> The present report’s finding that patients that received oseltamivir had a longer length of stay is largely accounted for by confounding, as this association was not found on adjusted analyses.

There are several limitations to this surveillance system. Not all cases of influenza in hospitals are diagnosed due to the lack of use of diagnostics, poor quality sample collection or delayed presentations. Surveillance data from other systems

documented intense interseasonal activity with notifications in March 2019 comparable to peak activity in 2018,<sup>27</sup> prior to FluCAN surveillance commencing in April. There are a number of potential confounders when considering the association between influenza hospitalisation and influenza vaccination, including confounding by indication, the healthy user effect, and confounding by frailty. Additionally, there are some concerns that other biases may be inherent to the test negative study design commonly used to assess vaccine effectiveness, although more recent data suggests that these may not result in significant bias.<sup>28,29</sup>

In summary, the 2019 FluCAN surveillance system detected a larger number of hospital admissions with laboratory-confirmed influenza in a national observational study than has been seen in recent seasons. Vaccination coverage appeared similar to previous seasons in adults, but increased in children. With the change in funding status, the adjuvanted vaccine was used most commonly in the elderly. Vaccine effectiveness in the target population and the elderly was moderate overall, but was particularly high in children.

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